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NEWS	3	FEB 28	PATDPAFULL - New display fields provide for legal status
			data from INPADOC
NEWS	4	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	5	MAR 02	GBFULL: New full-text patent database on STN
NEWS	6	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	9	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	10	MAR 22	PATDPASPC - New patent database available
NEWS	11	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	12	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	13	APR 04	EMBASE - Database reloaded and enhanced
NEWS	14	APR 18	New CAS Information Use Policies available online
NEWS	15	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAPLUS and
			USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS	16	APR 28	Improved searching of U.S. Patent Classifications for
			U.S. patent records in CA/CAPLUS
NEWS	17	MAY 23	GBFULL enhanced with patent drawing images
NEWS	18	MAY 23	REGISTRY has been enhanced with source information from
			CHEMCATS
NEWS	19	JUN 06	STN Patent Forums to be held in June 2005

NEWS 20 JUN 06 The Analysis Edition of STN Express with Discover!
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NEWS 21 JUN 13 RUSSIAPAT: New full-text patent database on STN
NEWS 22 JUN 13 FRFULL enhanced with patent drawing images
NEWS 23 JUN 20 MEDICONF to be removed from STN

NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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* * * * * STN Columbus * * * * *
* *

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FULL ESTIMATED COST	0.21	0.21

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=> S
ENTER LOGIC EXPRESSION, QUERY NAME, OR (END):src
L1 57667 SRC

```
=> s (Pas domain) (4A) Binding
L2      142 (PAS DOMAIN) (4A) BINDING

=> s (Pas domain) (4A) hydrophobic
L3      2 (PAS DOMAIN) (4A) HYDROPHOBIC

=> s (Pas domain) (4A) hydrophobic or core or nucleus or center
L4      2435166 (PAS DOMAIN) (4A) HYDROPHOBIC OR CORE OR NUCLEUS OR
CENTER

=> s (Pas (w) domain) (4A) (hydrophobic or core or nucleus or center)
3 FILES SEARCHED...
L5      7 (PAS (W) DOMAIN) (4A) (HYDROPHOBIC OR CORE OR NUCLEUS
OR CENTER)
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=> s l2 and l5
L6      2 L2 AND L5
```

```
=> duplicate
ENTER REMOVE, IDENTIFY, ONLY, OR (?):remove
ENTER L# LIST OR (END):l6
PROCESSING COMPLETED FOR L6
L7      2 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
```

```
=> d l7 1-2 bib ab
```

```
L7      ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
AN      2005:303296  CAPLUS
DN      142:351757
TI      Foreign PAS ligands regulate PAS domain function
IN      Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. a.;
Card, Paul B.;
        Harper, Shannon; Rutter, Jared; Bruick, Richard K.; McKnight,
Steven L.
PA      Board of Regents, the University of Texas System, USA
SO      U.S. Pat. Appl. Publ., 18 pp.
        CODEN: USXXCO
DT      Patent
LA      English
FAN.CNT 1
```

DATE	PATENT NO.	KIND	DATE	APPLICATION NO.
PI	US 2005074846	A1	20050407	US 2003-677734
20031001				
	WO 2005033662	A2	20050414	WO 2004-US32417
20041001				

```
W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
    CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
```

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
 KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
 NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
 ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
 ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
 DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,
 RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE,
 SN, TD, TG

PRAI US 2003-677734 A 20031001

AB Specific binding of a foreign **core** ligand to a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is determined by (a) detecting a first NMR spectrum of the PAS domain in the presence of a foreign ligand; and (b) comparing the first NMR spectrum with a second NMR spectrum of the PAS domain in the absence of the ligand to infer the presence the ligand specifically bound within the **hydrophobic core** of the **PAS domain**. A functional surface **binding** specificity of a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is changed by (a) introducing into the **hydrophobic core** of the **PAS domain** a foreign ligand of the PAS domain; and (b) detecting a change in the functional surface **binding** specificity of the **PAS domain**.

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:513152 CAPLUS

DN 141:50134

TI NMR detection of foreign PAS domain ligands

IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. A.; Card, Paul B.

PA Board of Regents, University of Texas System, USA

SO U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Pat. Appl. 2003

59,917.

CODEN: USXXCO

DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.
------------	------	------	-----------------

DATE

PI US 2004121409	A1	20040624	US 2003-677733
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20031001

US 6319679	B1	20011120	US 2001-770170
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20010126

US 2003059917	A1	20030327	US 2001-59962
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20011119

PRAI US 2001-770170	A3	20010126	
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US 2001-59962	A2	20011119	
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AB Specific binding of a foreign **core** ligand to a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no

NMR-apparent a

priori formed ligand cavity, is determined by (a) detecting a first NMR

spectrum of the PAS domain in the presence of a foreign ligand; and (b)

comparing the first NMR spectrum with a second NMR spectrum of the PAS

domain in the absence of the ligand to infer the presence the ligand

specifically bound within the **hydrophobic core** of the

PAS domain. A functional surface **binding**

specificity of a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and, comprises a hydrophobic core

that has no NMR-apparent a priori formed ligand cavity, is changed by (a)

introducing into the **hydrophobic core** of the

PAS domain a foreign ligand of the PAS domain; and (b)

detecting a change in the functional surface **binding** specificity of the **PAS domain**.

=> file stnguide

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

47.61

47.82

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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-1.46

FILE 'STNGUIDE' ENTERED AT 18:01:36 ON 23 JUN 2005

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jun 17, 2005 (20050617/UP).

=> d 14 1-2 bib ab

YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS' - CONTINUE? (Y)/N:y

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:303296 CAPLUS
DN 142:351757
TI Foreign PAS ligands regulate PAS domain function
IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. a.;
Card, Paul B.;
Harper, Shannon; Rutter, Jared; Bruick, Richard K.; McKnight,
Steven L.
PA Board of Regents, the University of Texas System, USA
SO U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO

DT Patent
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
US 2005074846	A1	20050407	US 2003-677734
WO 2005033662	A2	20050414	WO 2004-US32417

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,
RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE,
SN, TD, TG

PRAI US 2003-677734 A 20031001

AB Specific binding of a foreign core ligand to a PAS domain,
wherein the PAS

domain is predetd., prefolded in its native state, and comprises
a hydrophobic core that has no NMR-apparent a priori formed ligand cavity,
is determined by (a) detecting a first **NMR** spectrum of the **PAS domain** in the presence of a foreign ligand; and (b) comparing the first NMR spectrum with a second **NMR** spectrum of the **PAS domain** in the absence of the ligand to infer the presence the ligand specifically bound within the hydrophobic core of the PAS domain. A functional surface **binding** specificity of a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is changed by (a) introducing into the hydrophobic core of the PAS domain a foreign ligand of the PAS domain; and (b) detecting a change in the functional surface **binding** specificity of the **PAS domain**.

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:513152 CAPLUS
DN 141:50134
TI **NMR** detection of foreign **PAS domain** ligands
IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. A.; Card, Paul B.
PA Board of Regents, University of Texas System, USA
SO U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Pat. Appl. 2003

59,917.
CODEN: USXXCO

DT Patent
LA English
FAN.CNT 2

DATE	PATENT NO.	KIND	DATE	APPLICATION NO.
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PI	US 2004121409	A1	20040624	US 2003-677733
20031001				
	US 6319679	B1	20011120	US 2001-770170
20010126				
	US 2003059917	A1	20030327	US 2001-59962
20011119				
PRAI	US 2001-770170	A3	20010126	
	US 2001-59962	A2	20011119	

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=> file stnguide		
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
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 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Jun 17, 2005 (20050617/UP).

=>

=> d 15 1-7 bib ab

L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:303296 CAPLUS
DN 142:351757
TI Foreign PAS ligands regulate PAS domain function
IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. a.;
Card, Paul B.;
Harper, Shannon; Rutter, Jared; Bruick, Richard K.; McKnight,
Steven L.
PA Board of Regents, the University of Texas System, USA
SO U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

DATE	PATENT NO.	KIND	DATE	APPLICATION NO.
-----	-----	----	-----	-----
PI	US 2005074846	A1	20050407	US 2003-677734
20031001				
	WO 2005033662	A2	20050414	WO 2004-US32417
20041001				
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,			
CA, CH,	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,			
GB, GD,	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,			
KZ, LC,	LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,			
NA, NI,	NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,			
SL, SY,	TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,			
ZM, ZW				
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,			
ZW, AM,	AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,			
DE, DK,	EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT,			
RO, SE,	SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,			
MR, NE,				
	SN, TD, TG			

PRAI US 2003-677734 A 20031001
AB Specific binding of a foreign core ligand to a PAS domain,
wherein the PAS
domain is predetd., prefolded in its native state, and comprises
a
hydrophobic core that has no NMR-apparent a priori formed ligand
cavity,

is determined by (a) detecting a first **NMR** spectrum of the **PAS domain** in the presence of a foreign ligand; and (b) comparing the first NMR spectrum with a second **NMR** spectrum of the **PAS domain** in the absence of the ligand to infer the presence the ligand specifically bound within the hydrophobic core of the PAS domain. A functional surface binding specificity of a PAS domain, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is changed by (a) introducing into the hydrophobic core of the PAS domain a foreign ligand of the PAS domain; and (b) detecting a change in the functional surface binding specificity of the PAS domain.

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2004:513152 CAPLUS
 DN 141:50134
 TI **NMR** detection of foreign **PAS domain** ligands
 IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. A.; Card, Paul B.
 PA Board of Regents, University of Texas System, USA
 SO U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Pat. Appl. 2003

59,917.
 CODEN: USXXCO

DT Patent
 LA English
 FAN.CNT 2

DATE	PATENT NO.	KIND	DATE	APPLICATION NO.
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PI	US 2004121409	A1	20040624	US 2003-677733
20031001	US 6319679	B1	20011120	US 2001-770170
20010126	US 2003059917	A1	20030327	US 2001-59962
20011119	PRAI US 2001-770170	A3	20010126	
	US 2001-59962	A2	20011119	
AB	Specific binding of a foreign core ligand to a PAS domain, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is determined by (a) detecting a first NMR spectrum of the			

PAS domain in the presence of a foreign ligand; and (b)
 comparing the first NMR spectrum with a second **NMR** spectrum of
 the **PAS domain** in the absence of the ligand to infer
 the presence the ligand specifically bound within the
 hydrophobic core of
 the PAS domain. A functional surface binding specificity of a
 PAS domain,
 wherein the PAS domain is predetd., prefolded in its native
 state, and,
 comprises a hydrophobic core that has no NMR-apparent a priori
 formed
 ligand cavity, is changed by (a) introducing into the
 hydrophobic core of
 the PAS domain a foreign ligand of the PAS domain; and (b)
 detecting a
 change in the functional surface binding specificity of the PAS
 domain.

L5 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 1
 AN 2004119294 MEDLINE
 DN PubMed ID: 15009198
 TI The PAS fold. A redefinition of the PAS domain based upon
 structural
 prediction.
 AU Hefti Marco H; Francoijs Kees-Jan; de Vries Sacco C; Dixon Ray;
 Vervoort
 Jacques
 CS Laboratory of Biochemistry, Wageningen University, the
 Netherlands..
 marco@keydp.com
 SO European journal of biochemistry / FEBS, (2004 Mar) 271 (6)
 1198-208.
 Journal code: 0107600. ISSN: 0014-2956.
 CY Germany: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200404
 ED Entered STN: 20040311
 Last Updated on STN: 20040428
 Entered Medline: 20040427
 AB In the postgenomic era it is essential that protein sequences are
 annotated correctly in order to help in the assignment of their
 putative
 functions. Over 1300 proteins in current protein sequence
 databases are
 predicted to contain a PAS domain based upon amino acid sequence
 alignments. One of the problems with the current annotation of
 the PAS
 domain is that this domain exhibits limited similarity at the
 amino acid
 sequence level. It is therefore essential, when using proteins
 with

low-sequence similarities, to apply profile hidden Markov model searches

for the PAS domain-containing proteins, as for the PFAM database. From

recent 3D X-ray and **NMR** structures, however, **PAS domains** appear to have a conserved 3D fold as shown here by structural alignment of the six representative 3D-structures from the PDB

database. Large-scale modelling of the PAS sequences from the PFAM

database against the 3D-structures of these six structural prototypes was

performed. All 3D models generated (> 5700) were evaluated using prosaii.

We conclude from our large-scale modelling studies that the PAS and PAC

motifs (which are separately defined in the PFAM database) are directly

linked and that these two motifs form the PAS fold. The existing subdivision in PAS and PAC motifs, as used by the PFAM and SMART databases, appears to be caused by major differences in sequences in the

region connecting these two motifs. This region, as has been shown by

Gardner and coworkers for human PAS kinase (Amezcuca, C.A., Harper, S.M.,

Rutter, J. & Gardner, K.H. (2002) Structure 10, 1349-1361, [1]), is very

flexible and adopts different conformations depending on the bound ligand.

Some PAS sequences present in the PFAM database did not produce a good

structural model, even after realignment using a structure-based alignment

method, suggesting that these representatives are unlikely to have a fold

resembling any of the structural prototypes of the PAS domain superfamily

L5 ANSWER 4 OF 7 CABA COPYRIGHT 2005 CABI on STN

AN 2003:130562 CABA

DN 20033102640

TI The NifL PAS domain - insight into its structure and function

AU Hefti, M. H.

CS Wageningen University, Postbus 9101 6700 HB Wageningen, Netherlands.

SO The NifL PAS domain: insight into its structure and function, (2003) pp.

115. 332 ref.

Publisher: Wageningen Universiteit (Wageningen University). Wageningen

ISBN: 90-5808-809-X

CY Netherlands Antilles

DT Dissertation

LA English

SL Dutch

ED Entered STN: 20030812

Last Updated on STN: 20030812

AB This thesis contains 8 chapters focusing on the PAS domain of the nitrogen

fixation regulatory protein NifL from *Azotobacter vinelandii*.

PAS domains

are found in sensor proteins and are named after homology between the

Drosophila period protein (PER), the aryl hydrocarbon receptor nuclear

translocator protein (ARNT) and the *Drosophila* single-minded protein

(SIM). The first chapter provides a brief review on nitrogen fixation and

the biochemical importance of PAS domains. The NifL protein is a flavoprotein, with flavin adenine dinucleotide (FAD) as the prosthetic

group. The second chapter summarizes the tools currently available within

the field of flavoprotein deflavination and reconstitution. A new purification method for Histidine-tagged proteins is described in the next

chapter. On-column cleavage of the protein with thrombin facilitates the

separation of the protein of interest and the His-tag. In chapter 4, the

His-tag is again used as a tool to deflavinatate and reconstitute the NifL

PAS domain protein. Chapter 5 describes the current status of the structure elucidation of this domain, using X ray crystallography.

Small-angle X ray scattering (SAXS) studies with this domain clearly

showed the tetrametric state of the PAS domain. In an envelope, created

using SAXS data, four monomeric models of the PAS domain were fitted to

elucidate the structural arrangement of these four monomers (chapter 6).

In the next chapter, the term PAS fold is introduced to denote a three-dimensional fold present in several proteins. The 3D structures

determined of a PAS domain containing protein include: (i) the structure

of the *Ectothiorhodospira halophila* blue-light receptor photoactive yellow

protein; (ii) structure of the heme-binding domain of the rhizobial oxygen

sensor FixL from Bradyrhizobium japonicum and from Rhizobium meliloti; and

(iii) the N-terminal domain of the human ether-a-go-go-related potassium

channel HERG, the flavin mononucleotide containing phototropin module of

the chimeric fern Adiantum photoreceptor, and the average NMR structure of the N-terminal PAS domain of human PAS

kinase. Some concluding remarks are provided in the final chapter.

L5 ANSWER 5 OF 7 MEDLINE on STN

DUPLICATE 2

AN 2003611132 MEDLINE

DN PubMed ID: 14668441

TI Structural basis for PAS domain heterodimerization in the basic helix--loop--helix-PAS transcription factor hypoxia-inducible factor.

AU Erbel Paul J A; Card Paul B; Karakuzu Ozgur; Bruick Richard K; Gardner

Kevin H

CS Departments of Biochemistry and Pharmacology, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas,

TX 75390,

USA.

NC CA90601 (NCI)

CA95471 (NCI)

GM08297 (NIGMS)

SO Proceedings of the National Academy of Sciences of the United States of

America, (2003 Dec 23) 100 (26) 15504-9. Electronic Publication: 2003-12-10.

Journal code: 7505876. ISSN: 0027-8424.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200404

ED Entered STN: 20031225

Last Updated on STN: 20040421

Entered Medline: 20040420

AB Biological responses to oxygen availability play important roles in

development, physiological homeostasis, and many disease processes. In

mammalian cells, this adaptation is mediated in part by a conserved

pathway centered on the hypoxia-inducible factor (HIF). HIF is a heterodimeric protein complex composed of two members of the basic

helix-loop-helix Per-ARNT-Sim (PAS) (ARNT, aryl hydrocarbon receptor

nuclear translocator) domain family of transcriptional activators,

HIF α and ARNT. Although this complex involves protein-protein interactions mediated by basic helix-loop-helix and PAS domains in both proteins, the role played by the PAS domains is poorly understood. To address this issue, we have studied the structure and interactions of the C-terminal **PAS domain** of human HIF-2 α by **NMR** spectroscopy. We demonstrate that HIF-2 α PAS-B binds the analogous ARNT domain in vitro, showing that residues involved in this interaction are located on the solvent-exposed side of the HIF-2 α central beta-sheet. Mutating residues at this surface not only disrupts the interaction between isolated PAS domains in vitro but also interferes with the ability of full-length HIF to respond to hypoxia in living cells. Extending our findings to other PAS domains, we find that this beta-sheet interface is widely used for both intra- and intermolecular interactions, suggesting a basis of specificity and regulation of many types of PAS-containing signaling proteins.

L5 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:729661 CAPLUS

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TI Structural basis of a phototropin light switch

AU Harper, Shannon M.; Neil, Lori C.; Gardner, Kevin H.

CS Departments Biochemistry and Pharmacology, Univ. Texas Southwestern

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SO Science (Washington, DC, United States) (2003), 301(5639), 1541-1544

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PB American Association for the Advancement of Science

DT Journal

LA English

AB Phototropins are light-activated kinases important for plant responses to

blue light. Light initiates signaling in these proteins by generating a

covalent protein-FMN adduct within sensory Per-ARNT-Sim (PAS) domains. We

characterized the light-dependent changes of a phototropin **PAS domain** by solution **NMR** spectroscopy and found that an

α helix located outside the canonical domain plays a key role in this activation process. Although this helix assoc. with the

PAS core in

the dark, photoinduced changes in the domain structure disrupt this interaction. We propose that this mechanism couples light-dependent bond formation to kinase activation and identifies a signaling pathway conserved among PAS domains.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 3
AN 2002619803 MEDLINE
DN PubMed ID: 12377121
TI Structure and interactions of PAS kinase N-terminal PAS domain:
model for
intramolecular kinase regulation.
CM Comment in: Chem Biol. 2002 Nov;9(11):1165-6. PubMed ID: 12445766
AU Amezcua Carlos A; Harper Shannon M; Rutter Jared; Gardner Kevin H
CS Department of Biochemistry, The University of Texas Southwestern
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Center, Dallas, TX 75390, USA.
NC CA-90601 (NCI)
SO Structure (Cambridge, Mass. : 2001), (2002 Oct) 10 (10) 1349-61.

Journal code: 101087697. ISSN: 0969-2126.
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DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS PDB-1LL8
EM 200304
ED Entered STN: 20021015
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AB PAS domains are sensory modules in signal-transducing proteins
that
control responses to various environmental stimuli. To examine
how those
domains can regulate a eukaryotic kinase, we have studied the
structure
and binding interactions of the N-terminal **PAS domain**
of human PAS kinase using solution **NMR** methods. While this
domain adopts a characteristic PAS fold, two regions are
unusually
flexible in solution. One of these serves as a portal that
allows small
organic compounds to enter into the core of the domain, while
the other
binds and inhibits the kinase domain within the same protein.
Structural
and functional analyses of point mutants demonstrate that the
compound and
ligand binding regions are linked, suggesting that the PAS
domain serves

as a ligand-regulated switch for this eukaryotic signaling system.

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